Specification

Please amend the specification as follows:

At page 1, line 15 amend 2,5 to 2.5

At page 2, line 28 amend "advantage being manifest particularly" to advantage is manifested particularly.

REMARKS

Claims 13-20 are pending in the instant application. Applicants have not raised any issues of new matter.

Claims 13-20 have been rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 13-23 of U.S. Application No. 10/754,685, and over claims 13-19 of U.S. Application No. 10/754,732.

Claims 13-20 have been rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 6,514,958, and over claims 1-11 of U.S. Patent No. 6,399,594.

Applicants will submit terminal disclaimers to overcome such rejections as both this application and the cited applications and patents are commonly owned by the same assignee.

SPECIFICATON

The Examiner has alleged that the incorporation by reference of EP 389 035 is improper. Applicants respectfully traverse that rejection. The incorporation by reference of EP 389 035 is for the general information of compositions having tibolone with a pharmaceutically acceptable solid carrier, not as a limitation on the invention.

Applicants will amend the specification in reference to the trademark LIVIAL® prior to issuance of this application.

35 U.S.C. 103 REJECTION

The Examiner alleges that the present invention is obvious in view of Kelder et al. (US 4,701,450) taken together with 'Stedman's Medical Dictionary' (1972, page 589),'Handbook of Pharmaceutical Excipients' (1986, pages 108-110, 259-260 and 289-293), Loliger et al. (US 5,364,886) and Sas et al. (EP 389035).

Applicants respectfully traverse this objection. In the present application, it was surprisingly found that increasing the amount of starch used in the carrier serves as a novel method of making a dosage unit comprising tibolone with improved stability (specification page 2, lines 4-5) and furthermore said dosage units were found to have improved storage properties in a humid atmosphere (specification page 1, lines 24-25).

The Examiner has pointed to the many elements missing from the disclosure in the cited prior art and then using impermissible hindsight, attempts to reconstruct the invention from the prior art. There is nothing in the teachings of the cited prior art that in anyway addresa the question of improved stability and/or storage. One looking to the question of stability and/or storage would not be led to the cited prior art to solve the problems with regard to such stability and/or storage.

None of the cited documents, either alone or in combination, teach or suggest the pharmaceutical dosage unit of the subject application with a carrier having at least 10-40% by weight of starch and wherein the dosage unit is maintained in an atmosphere of 50-75% relative humidity until administration. The resulting dosage units, comprising tibolone with improved stability, are illustrated at least by Examples 5,6,7 and 11 (pages 9-11 and 13) of the subject application.

The Examiner considers that conditions of 50% to 75% relative humidity would be expected to occur at any storage temperature depending on atmospheric pressure. Applicant submits that regulatory authorities stipulate storage at controlled temperature and humidity conditions. This is achieved in practice by storing at a constant temperature and having a system which can maintain a near overall constant level of relative humidity with small changes in atmospheric pressure. Applicant submits that without such a control, conditions may vary between a humid atmosphere (defined by 50% to 75% relative humidity) and a dry atmosphere(45% relative humidity or below) in view of fluctuations in atmospheric pressure. The carriers of the subject application comprising 10-40% of starch when stored in a humid atmosphere (50-75% relative humidity) were found to have improved stability compared to when said carriers were stored in a dry atmosphere (see, for example, Example 5, page 9 of the subject application). This improved stability is made possible when the humid conditions are carefully maintained in accordance with the subject invention. Furthermore the art teaches away from the present invention in that it is known in the art that moisture can often lead to poorer storage and greater decomposition of pharmaceutical compositions. The discovery in the present invention that humid conditions are preferred for storage over dry conditions is therefore unexpected.

Kelder et al. (US 4,701,450) teaches that pharmaceutically acceptable carriers comprising tibolone can be composed of one or more of a number of possible ingredients (col.3, lines 7-16). Applicant fails to see in Kelder et al. any teaching or suggestion of improved stability of the pharmaceutical dosage unit of the current invention resulting from the carriers comprising 10-40% by weight of starch in the carrier and maintaining the dosage unit in a humid atmosphere of 50-75% relative humidity until administration.

Further, at least for the reasons below, even assuming arguendo the combination of the other references with Kelder et al., the deficiencies of that reference are not cured.

As to the Examiner's assertions with respect the 'Handbook of Pharmaceutical Excipients', Applicant fails to see any teaching or suggestion of use of starch to impart improved stability to pharmaceutical formulations, let alone to pharmaceutical

formulations of tibolone, or to maintain such formulations in the humid condition of the current inventions. Hence the "Handbook" does not remedy the deficiencies of Kelder et al.

Turning to Loliger et al. (US 5,364,886 and Sas et al. (EP 389035), Applicant fails to see any teaching or suggestion of the use of 10-40% by weight starch in the carrier and maintaining the dosage unit at 50-75% relative humidity. Thus the requirements lacking in Kelder et al. are not met by these references.

Conclusion

Applicants submit that every issue raised by the outstanding Office Action has been addressed and rebutted. Applicant respectfully submit that the present claims define patentable subject matter and are in condition for allowance.

Should the Examiner believe that a conference would be helpful in advancing the prosecution of this application, he is invited to telephone Applicants' Attorney at the number below.

Respectfully submitted,

David H. Vickrey
Attorney for Applicant(s)
Reg. No. 30,697

Akzo Nobel Inc.
Intellectual Property Department
7 Livingstone Avenue
Dobbs Ferry, NY 10522-3408
Tel No.: (914) 674-5460